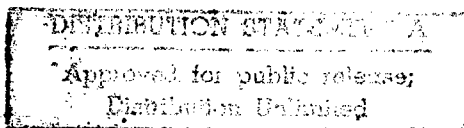


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DETERMINATION AND PLASTICITY OF SKIN UNDER NORMAL,  
EXPERIMENTAL, AND PATHOLOGICAL CONDITIONS

- USSR -

by Ye. Sh. Gerlovin

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DETERMINATION AND PLASTICITY OF SKIN UNDER NORMAL,  
EXPERIMENTAL, AND PATHOLOGICAL CONDITIONS  
(On Results of the Seventh Conference Dedicated  
to the Memory of Academician A. A. Zavarzin)

[This is a translation of an article by Ye. Sh. Gerlovin in Arkhiv Anatomii, Gistologii i Embryologii (Archives of Anatomy, Histology, and Embryology), No 12, Moscow/Leningrad, December 1959, pages 104-118.]

On 15 to 18 April 1959 the Seventh Scientific Conference dedicated to the memory of the founder of evolutionary histology, Academician Aleksey Alekseyevich Zavarzin took place in Leningrad. The Conference was dedicated to the most important problem of modern histology and embryology -- the determination and plasticity of tissues under normal, experimental, and pathological conditions. Various concepts exist in modern science of the determination and plasticity of tissues. Some researchers think that the tissues are very conservative and that their nature is determined by the history of development, others admit wide intertissue transformations. The solution of this problem is of great importance to the correct understanding of changes in human tissues under pathological conditions, especially in tumor growth, inflammation, and other processes.

The Conference was organized by the Military-Medical Order of Lenin Academy imeni S. M. Kirov and by the Leningrad Section of the All-Union Scientific Society of Anatomists, Histologists, and Embryologists. The program included 54 reports and 27 demonstrations. The program was sent out in due time to the participants of the Conference, and before the very start of the Conference theses of the reports and demonstrations were issued (volume of 7.5 printed sheets) (1) A fact which made possible a full-value discussion of not only the reports but the demonstrations as well.

(1) Theses of reports of the Scientific Conference on the Problem of Determination and Plasticity of Tissues under normal, Experimental and Pathological Conditions dedicated to the Memory of Academician A. A. Zavarzin (15-18 April 1959). Editor -- Corresponding Member of the Academy of Medical Sciences, Professor S. I. Shchelkunov, Leningrad, 1959

About 300 scientific workers and physicians participated in the work of the Conference (embryologists, histologists, anatomists, pathologo-anatomists, physiologists, patho-physiologists, zoologists, etc.), including 67 visitors from 23 cities of the country (Moscow, Baku, Vladivostok, Dnepropetrovsk, Yerevan, Ivanovo, Kaunas, Kazan', Memerovo, Karaganda, Minsk, Novosibirsk, Odessa, Orenberg, Perm', Ryazan', Rostov-on-Don, Samarkand, Smolensk, Tartu, Khar'kov, and Ul'yanovsk).

Forty-three reports were submitted during the six scientific meetings (of these -- 39 program-reports, and four reports were included in the program during the Conference). Thirty-one demonstrations were exhibited (15 demonstrations in connection with the above-mentioned reports and 16 demonstrations which had been included in the program).

The Conference was characterized by great activity of its participants to which attested numerous discussions (41 speakers).

An important element was the organization of problem sessions and the development of keen, principal discussions on the most debatable problems which were of a comradely character and contributed to a thorough and creative discussion of the reports.

The Conference opened in the auditorium of the anatomy building of the Military-Medical Order of Lenin Academy imeni S. M. Kirov in which Academician A. A. Zavarzin has lectured to students for many years and presented scientific reports at the sessions of the Leningrad Scientific Society of Anatomists, Histologists, and Embryologists which he had founded. On a red cloth was the portrait of Academician A. A. Zavarzin surrounded with flowers.

In opening the Conference, Deputy-Director of the Academy, Corresponding Member of the Acad Sci USSR Prof. A. N. Maksimenkov noted that Academician Zavarzin had headed the Chair of Histology of the Military-Medical Academy for 15 years. As an alumnus of St. Petersburg University, A. A. Zavarzin was the first to introduce an evolutionary approach to the study of tissues and created a new original direction in biological science -- evolutionary histology.

The studies of Zavarzin represent a striking example of the combination of the interests of theory and practice in medicine and biology. A scientist of principle, who firmly believed in the power of science and the power of theory based on authentic facts, A. A. Zavarzin was at the same time a great organizer. While still a young scientist, he played a large part in the organization of the Chair of Histology at Perm' University. At the suggestion of the chairman the participants of the Conference honored the memory of Academician A. A. Zavarzin by rising.

The first session was devoted to the problem of determination in histology and embryology.

The report "Determination as the Central Problem of

Experimental Embryology" was submitted by Corresponding Member of the Acad Sci USSR, Prof. Svetlov (Leningrad). While histologists contrast determination to plasticity as properties of tissues, embryologists regard determination as a process, a motive force of development, a leading vital system toward a definite determined state. A system is determinative when it possesses a formed complex of factors which determine the specificity of its final state (which can be the end result of a stage or phase of development). Whereas, during the era of the predominance of the mosaic theory of development, determination was regarded as a negative concept leading to the limitation of potency, as a change occurring momentarily during the act of cell division, at the present stage of science determination must be interpreted as a process which determines the path of differentiation of a system toward the end of one or another stage (phase) of development. This process has a gradual character and takes place during the so-called critical periods of development, i.e., the initial segments of the important, physiologically isolated stages of ontogenesis and its components. Therefore, determination is a transition to the acquisition of new properties, new characteristics. In order to effect the transition from a non-determined state to a determined one, an external influence is needed. Cellular determination is a special case of determination. The determination concept is changed from a negative concept to a positive one, and its bond with the potency of development is severed. The speaker thinks that the idea of limitation of the morphogenetic potencies of tissues and their specificity becomes an empirical fact devoid of theoretical meaning and that metaplasia becomes a phenomenon principally possible. The absence of limitations of potency in the genome of tissue cells is postulated in the modern theory of heredity.

Corresponding Member of the Acad Med Sci USSR S. I. Shchelkunov (Leningrad) noted in his report "Data on the Study of Determination of Tissues and their Importance to Evolutional Histology and Medicine" that modern Histology studies mainly the rules of structure and function of tissue structure in their post-embryonic period of development. One of the basic problems of histology is the study of development of tissues during the entire ontogenesis, including the development of provisory tissues. In histology and embryology determination must be understood as the definite qualitative state of the developing cellular material as it is represented by embryos and tissues at various stages of ontogenesis. In the study of determination of tissues up to recent times there has been insufficient attention paid to the significance of integration of tissues within the organism and to the role of environment in this process. Since at the basis of structure determination and their historical conditioning lies the inheritance

of their intrinsic characteristics of structure and properties, it must also be regarded in its genetic aspect. Of special interest in this respect is the study of inherited information on the molecular level, for it is effected during the process of cellular division. Thus, determination of tissues is the result of realization of hereditary information during ontogenesis. The tissue development is mutually conditioned and determined, first of all, by the rules of ontogenesis which are reflected in a number of symptoms, including heterochronia (which represents the adaptation of tissues to developmental conditions), and in the appearance of various gradients in the developing tissues. The data of the study of determination of tissues, their plasticity and reactivity are the key to the decoding of various complicated tissue changes under pathological conditions, including the growth of tumors. The basic theses of the report were illustrated with facts from the works of the author and his associates.

Determination and plasticity of the extraembryonic mammalian tissues under normal, experimental, and pathologic conditions were the subject of the report of Prof. M. Ya. Subbotin (Novosibirsk).

A comparative study of the provisory organs of mammalia conducted by the author by means of regular histological and histochemical methods shows that even at early stages of embryogenesis the extraembryonic tissues represent highly specialized structures, and that their development is determined in a definite way. The author's data corroborated the findings of S. I. Shchelkunov (1958) on the asynchronous development of tissues of provisory and definitive organs. The trophoblast is transformed very early into a chorionic symplastic epithelium, which is connected with the development in the latter of a complex enzyme system, thus ensuring its muco- and proteolytic functions. Under pathological conditions, for example, in aseptic inflammation the human placenta, as well as the placenta of rodents, manifests considerable specialization and does not change into other tissues. The author subjected to particular criticism the views of certain authors on the formation of neural elements from the placental connective tissue. The speaker emphasized the fact that the perifetal fluids are the result of secretion of the amniotic epithelium which also effects their resorption. However, the provisory structures manifest also certain plasticity under experimental and pathological conditions. Of considerable interest in this context are the speaker's experiments with transplantation of the amniotic epithelium on the mucosa of the esophagus (where it perishes) and in place of the serous membrane, under conditions of aseptic inflammation, where it manifests plastic properties and assumes the structure of multilayer flat epithelium similar to the corneal epithelium of the eye. The extraembryonic mesenchyma changes at the early stages of pregnancy into highly specialized and determinate tissues and forms

smooth muscular cells within the composition of the amnion and the umbilical cord, while under pathological conditions it manifests changes in the fibroblast system which are accompanied by the accumulation of high-polymeric acid mucopolysaccharides in the interstitial substance.

Prof. A. G. Knorre (Leningrad) in a report "Problem of Tissue Determination and Means of its Development" subjected to criticism the contention of V. G. Yeliseyev (1953) that the teaching of determination indicates only the qualitative peculiarity of tissues and organs and has nothing in common with the philosophical teaching of determinism. The teaching of determination tissue properties represents a concretization (in the histological field) of the principle of philosophic determinism -- one of the most important principles of dialectic materialism. "Histological transformism" (admission of unlimited intertissue transformations) is a manifestation of philosophical non-determinism. The teaching of tissue determination has nothing in common with preformism. Tissue determination is a process of a causative definition (conditioning, reinforcing) of the ways of development of the cellular material of embryonic rudiments which leads to the emergence of definite tissue derivatives. Determination can be labile at

first and later become non-reversible. According to A. G. Knorre, one can not counterpose determination to "plasticity." Determination, similarly to heredity, implies a definite range of mutability. Tissue determination does not imply the exhaustion of possibilities of development and the appearance of immutable characteristics; it only implies that further change becomes possible not in all directions but only in definite, historically conditioned ones. Parallel with this, determination presupposes the emergence of new possibilities of development which are absent in the non-determined cellular material. From the statement of facts of tissue determination it is time to switch to the study of factors (causes and conditions) of tissue determination in employing particularly for this purpose the cyto- and histo-chemical methods of investigation. The speaker mentions possible means of affecting determination processes in the interests of medical and national economy practice.

During the discussion period Prof. V. G. Yeliseyev (Moscow) stated that the discussion must not have a recrimination character, but that of friendly arguments. The speaker is in accord with P. G. Svetlov's opinion that determination is connected not with prospective potency, but with the prospective significance. Under changed conditions the potencies of cells undergo changes. In debating with Shchelkunov, Yeliseyev stated that mesenchyma is not a single but an aggregate rudiment which is formed from the material of the mesoderm, ectoderm, and neural tube. The smooth muscular tissue must be regarded in conjunction with all other contractile

tissues. In the development of smooth musculature from connective tissue a metaplastic process takes place. It is necessary at present to study the mutability of tissues and means of controlling tissue preactions, using for this purpose the hormones in particular.

Prof. B. Yu. Abraytis (Kaunas) emphasized the point that determination is conditioned not only by hereditary information but by the interdependence of tissues as well. Under pathological conditions one observes a considerable plasticity of the eye epithelium. A. Ya. Friedenshteyn (Moscow) called attention to the necessity of the study of factors of histogenesis. I. G. Mikhaylov (Leningrad) and L. K. Titova dwelt on the problem of study of provisory tissues in particular. L. K. Titova expressed critical remarks on the report of Prof. M. Ya. Subbotin in connection with the histochemical analysis of changes in the placenta. Ye. Sh. Gerlovin (Leningrad) noted that the problem of determination and tissue specificity had been extensively studied in recent years. A thorough study of the mutability and plasticity of tissues is needed in the future. Evolutional transformations of tissues take place in connection with the adaptation of organisms to new conditions of development, depending on their function. In this respect the phenomena of differentiation of tissue structures in certain specialized animals are of interest (for example, horny teeth in the oral cavity of lampreys, frog tadpole, etc.). In order to study the changes in the structure and functions of tissues it would be of great interest to undertake the development of methods of chronic, continuous effect of various factors on tissues. This principle is employed in experimental oncology to cause malignization of tissues.

In summarizing the first session, the chairman L. N. Zhinkin called attention to the fact that in the study of determination a historical approach is essential and that it is necessary to devote more study to the interrelation of cellular and tissue determination.

The second session was devoted to various methods of study of determination and plasticity of tissues.

In the report of Prof. S. Ya. Zalkind and L. P. Izakova (Moscow) "The Problem of Tissue Determination of Transplanted Cellular Strains" were cited data on the tissue determination of single layer cultures of transplanted cellular strains which had been cultivated outside the organism for various, at times prolonged periods. In order to elicit the tissue stability of certain strains of transplanted cells, the authors subjected three strains of transplanted cells to a comparative cytological and cytochemical analysis -- two strains from tumor cells (HE-Ia and HEP<sub>2</sub>) and one peculiar culture obtained from normal cardiac cells of macaque *tsinomol'gus* (SOTa). Analysis of the material showed that, parallel with certain similar traits, the studied cultures possess also specific traits which enable one to identify the culture from a few

isolated cells. In this respect, of particular interest is the dynamics of their mitotic activity. Each of the studied cultures possesses considerable tissue stability which attests to the presence of tissue determination. The report was beautifully illustrated with microphotos and color pictures.

In the report of Prof. V. P. Mikhaylov (Leningrad) "Manifestation of Tissue Determination in Cultures from Trypsin-Treated Tissues" were presented data on the cultivation of isolated, by means of trypsin, cells of various tissues in a liquid nutritive medium. Such "single-layer" cultures are widely used in obtaining virus suspensions in large quantities, which are needed for the preparation of vaccines and for virus diagnostics. The study of cultures from trypsin-treated tissues represents considerable interest from the point of view of clarification of tissues determination, for in such cultures the integrating effect of a whole organism is eliminated, as well as the intertissue and organ correlations. The growth zone in trypsin-treated cultures is formed not from a part of an organ but multicentrically -- from separate isolated cells. Under conditions of trypsin-treated single-layer cultures the tissues manifest their specific characteristics in the same manner as under the usual methods of cultivation. The speaker demonstrated interesting preparations on the effect of poliomyelitis virus on single-layer cultures.

During the debate Prof. Zaslavskiy (Moscow) related factual data on the cultivation of kidney epithelium in which, following a passage, three types of cells are distinguished which markedly differ from each other and which, presumably, develop from different sections of the nephron. There is a possibility of obtaining pure strains of isolated series of the above mentioned cells.

S. I. Shchelkunov noted the great interest of V. P. Mikhaylov's report in regard to the growth of isolated cells in trypsin-treated cultures and mentioned the fact that in his experiments with the removal of the surface corneal layers within the organism he had observed the growth of remaining isolated cells on the surface of the wound. Such cells formed single-layer flat elements which covered the surface of the wound and, subsequently, rapidly perished.

Prof. Ya. A. Ninnikov (Leningrad) took the floor in regard to Prof. Zalkind's report and emphasized the great importance of the method of tissue cultures at the present time. Back in the 30's our country was the first in the world in its work with tissue cultures, but in later years we were somewhat lagging in this field. At present the situation is straightening itself out, and this trend of investigations is developing at a more rapid pace. Not only the potencies of tissues are studied but these works are utilized in the interests of practice for the preparation of anti-virus vaccines. The peculiarities of the progeny of cellular



generations are studied. In regard to the report of Prof. Mikhaylov, Ya. A. Vinnikov noted that the speaker was the first in the country to employ the method of single-layer trypsin-treated cultures and to obtain a number of interesting facts. S. Ya. Malkind also highly evaluated the report of Prof. Mikhaylov and the importance of the work which he had accomplished.

Of considerable interest was the report by Prof. T. A. Grigor'yeva (Moscow) "On the Neurogenic Factor of Tissue Differentiation" in which large factual material was presented on tissue changes following their sensory denervation. The speaker stressed the point that differentiation, the acquisition of specific properties by tissues is the expression of tissue integration within the composition of the whole organism. A sensory neuron not only ensures establishment of the unity of the organism with the environment and the integration of parts of the organism into a unified system, but it also plays a large role in maintaining the structural wholeness and an adequate differentiation of the sections of the organism which it innervates. In the deafferentation of organs (effected by means of extirpation of the corresponding spinal cord ganglia) the latter develop, on one hand, a general reaction in the form of inflammation, and, on the other, a de-differentiation of its cellular elements and desintegration of tissues in the denervated organs. On the basis of the above stated, T. A. Grigor'yeva advanced a thesis that the methods of tissue cultivation are not applicable to the study of problems of evolution of tissues, since under these conditions the integration of the organism is eliminated, and since the theory of tissue evolution must be based on the analysis of tissue changes within the structure of the organism (as a biological unit) and on taking account of the integrating role of the nervous system.

During the debate, Prof. K. A. Lavrov (Rostov-on-Don) stressed the fact that the data of the Grigor'yeva report are of great general biological, neurological, and general pathological interest. Desintegration is a process in pre-tumor conditions, for the tumor does not participate in the life activity of the organism. V. P. Mikhaylov thinks that changes in deafferentation are close to dystrophic processes. The data of the report are also of considerable importance to general pathology. A. G. Knorre stressed the fact that in sensory deafferentation the level of tissue differentiation is reduced, but "is the determination of tissues removed in this process?" According to Knorre, the answer to this question can be obtained through the analysis of changes of deafferentiated tissues precisely under conditions of tissue cultures.

Ya. A. Vinnikov, having given a positive evaluation of the Grigor'yeva report, was not, however, in agreement with the speaker's statement regarding the importance of the method of tissue

cultures in evolutionary histology. S. Ya. Zalkind noted that pictures presented in the report resemble very much the single-layer tissue cultures. In his opinion, these works must be combined with the methods of tissue cultures by cultivating the deafferentated tissues in two ways: a) inoculating with tissue segments where tissue interrelations have been preserved and b) inoculating with trypsin-treated tissues where the cells are isolated and depend on themselves only.

S. I. Shchelkunov noted that a large amount of data has been presented in the reports for the understanding of tissue determination. In dwelling on the report of Prof. Grigor'yeva, he expressed accord with the statement that organic integration determines the trend of tissue development.. However, parallel with neural integration there also exists an exchange integration which originates during the ontogenesis prior to the formation of the nervous system. Otherwise it would be difficult to explain the healing of skin transplants which remain non-innervated for a long time.

In her concluding statement, Prof. Grigor'yeva stressed the fact that the method of tissue culture is of great importance in the study of a number of problems, cytological in particular, where it is necessary at times to separate the cell from the tissues. The use, however, of tissue culture methods for the evolutionary histological analysis of tissues is of no value since the tissues are studied without organic integration.

The report of the Corresponding Member of the Acad Sci USSR, Prof. P. V. Makarov (Leningrad), was devoted to seasonal and age-related changes of amphibian ovaries. Various cytochemical as well as autoradiographic methods were employed in this work (via administration of  $S^{35}$  methionine and  $P^{32}$ ). During the period of highest vital activity (July -- August) the protein synthesis proceeds most actively in all oocytes which are able to reach the state which ensures their ovulation the following spring. In September or early October the protein synthesis ceases in all oocytes, with the exception of the largest ones, and their growth is arrested. The author demonstrated also the changes in the activity of the enzymic systems of the oocytes depending on their size and season and expressed an opinion that RNA serves as source of energy, the "fuel" in the intracellular protein synthesis. The report was accompanied by a demonstration of preparations and radioautographs.

The report of Ya. A. Vinnikov (Leningrad) "Change in the Distribution of Oxidating Enzymes in the Mitochondria of Certain Cells as Indicator of their Reactivity" showed that following the action of various stimuli on capillary cells of the inner ear, neurons, the epithelium of the anterior wall of the crystalline lens, and the striated muscle fibers, a definite degree of activity of enzymes of the Krebs oxidation cycle is observed (succinate dehydrogenases and cytochrome oxidases) in the mitochondria. On this basis, one

can infer the level of the oxidizing respiration which represents the source of energy for cellular vital activity. Under the effect of adequate and non-adequate stimuli (sound, rotation, electric shock, injury and reparation) one observes, first, a marked rise in the content of succino-dehydrogenase and cytochrome in the mitochondria, with subsequent reduction of enzymic activity and its final restoration. The author stressed the point that various influences on a cell cause reactive metabolic exchanges, of the oxidizing respiration in particular, which ensure the energy for cellular processes.

Prof. V. V. Portugalov (Moscow) in a report "Certain Problems of Physiology of Mitochondria" came to the conclusion, based on the use of certain salts of mono- and di-terazols and the study of activity and distribution of succino-dehydrogenase in the mitochondria of the neural cells of various sections of the nervous system and other tissue cells in cats and rats in various irritations and pathological conditions, that under conditions of enhanced functional activity of the cell the intensity of oxidation processes in the mitochondria rises and the mitochondria themselves undergo changes. Under pathological conditions a reduction of enzymic activity takes place in some mitochondria while others may show increased activity and change in their size and shape. The speaker thinks that the change in the enzymic activity of cell mitochondria reflects on the whole selfregulating mechanism of a living system directed toward compensating the deficit in the energy balance of the cell caused by inactivation of part of the enzyme-active protein of the mitochondria.

P. V. Makarov subjected to criticism Portugalov's interpretation of the distribution of mitochondria. He thinks that the idea of septa is based on electronic microscopic studies, that it is a concept based on submicroscopic data and that it is impossible to arrive at conclusions based on a study with a luminous microscope. Ya. A. Minnikov noted that Portugalov's work corroborates his already published data on the distribution of succinhydrase in the mitochondria obtained in treating the preparations with neotetrazol.

A considerable interest was created by the report of Prof. O. Ye. Vyazov, B. V. Konyukhov, R. F. Averkin, and I. I. Titov (Moscow) devoted to the use of antigenic analysis in the study of tissue evolution. The authors showed on the basis of the antigenic analysis of the crystalline lens of vertebrate and non-vertebrate animals and of the lens formed as a result of Wolf regeneration, that organs performing similar functions and, consequently, finding themselves in similar environmental relations possess similar antigenic properties in spite of differences of origin. These data corroborate the theory of parallel Zavarzin series. However, parallel with the findings of these authors, there has been demonstrated the presence of two types of organo-specific antigens:

Antigens characteristic for the same organs of various species (reflecting the parallel character of organic specificity) and antigens inherent in a definite organ of representatives of a given animal species only and conditioned by the divergent antigenic organic specificity of a given species. The basic idea of the report consisted of the attempt to reconcile the A. A. Zavarzin theory of parallel series of tissue evolution with the N. G. Khlopin theory of divergent tissue evolution. P. V. Makarov noted that the philogenetic premises of the speakers were not sufficiently convincing because the phylogenesis of vertebrate animals has not been taken into consideration in their work and that only certain lateral branches were used. V. P. Mikhaylov stressed the importance of the thesis of the report of Vyazov and co-workers devoted to the boundary problem between immunology and histology, and recommended that the authors investigate the antigenic properties of striated muscles in frogs under various functional conditions (the motor musculature of the heart and lymphatic centers). He also called attention to the fact that Zavarzin had spoken not only of the parallelism of the histological structures but of the parallelism on the protein level as well, which is corroborated by data in the report. Ya. A. Vinnikov stressed the point that the great interest of Vyazov's report consists in the confirmation of the specificity of tissues by the immunological method.

In closing the second session the chairman Prof. A. L. Shabadash (Moscow) stressed the fact that reports demonstrated the unity of theory and practice. Various systematic means and approaches were employed in the reports: the usual explanation, explanation of trypsin-treated tissues, study of the antigenic properties of tissues, and the study of tissues in deafferentation. The trend to penetrate the chemistry of processes is common to all submitted reports. Of importance is the enzyme which ensures the energy to a developing cell. The presence of ribonucleoproteids is the key to the understanding of determination of cells. At present, ways are being outlined of changing the determination of cells and tissues by means of altering the type of metabolism, particularly of enzymes and mitochondria.

The third and fourth sessions (16 and 17 April) were devoted to determination and plasticity of epithelial tissues, especially of the cutaneous epithelium and its derivatives. The interesting report of Prof. L. N. Zhinkin (Leningrad) "Dynamics of Protein Metabolism in the Cutaneous Epithelium and the Crystalline Lens of White Rats" showed in a detailed presentation based on the employment of histoautoradiographic methods that on intensified synthesis of sulfur-containing proteins of the cutaneous epithelium is observed in cells of the horny layer long before the appearance of morphological signs of keratosis. A selective accumulation of  $S^{35}$  methionine was observed, which can change into cystine thus retaining

its radiosulfur. On the basis of the fact that radiosulfur bound with proteins is transferred to cells of the horny layer, the author was able to ascertain the rate of the physiological regeneration of the epidermis. At the same time the intensity of the protein metabolism by various epithelial layers and the character of radiosulfur accumulation in ontogenesis were elicited. The obtained data were compared with the distribution of  $S^{35}$  methionine during the development of the derivative of cutaneous ectoderma, the crystalline lens (experiments of S. G. Lebedeva); common properties of selective accumulation of radiosulfur were elicited in the cutaneous epithelium and the lens. The selective accumulation appears earlier than the functional activity of the skin or eye. All this indicates the determination of tissues which is expressed in morphological as well as biochemical phenomena.

During the debate Prof. S. I. Shchelkunov noted the importance of Prof. Zhinkin's report, since, by means of the employment of the autoradiographic method, convincing facts have been obtained which indicated the metabolic changes during the process of development of the cutaneous epithelium and the crystalline lens.

In a report by A. A. Zavarzin Jr (Leningrad) data were presented on experimental histological study of the biological properties of the epidermis and connective tissue of white rats embryos (age: 16th day of embryogenesis and up to birth). The speaker studied the regeneration of these tissues in 16-day old embryos (for five days following injury) and their regeneration 24 hours after injury in embryos of various ages and under conditions of transplantation of the skin of 16 days old embryos on the amniotic membrane of a 13-day old embryo. Parallel with histological methods of study a histo-autoradiographic analysis of the metabolism of sulfur containing proteins was made. The obtained data made possible the elicitation of certain biological peculiarities of the embryonal epidermis and its underlining connective tissue and to observe substantial age-connected changes in cutaneous tissue properties during the embryonal period, which manifested itself particularly clearly in the eave-like character of changes in mitotic activity and in the metabolism of sulfur-containing proteins. The work was carried out within the plan of studies outlined by Academician A. A. Zavarzin on age-related dynamics of tissues and corroborates his theoretical ideas on this subject. The report was accompanied by a large exhibit of histological preparations and histoautographs.

During the debate Prof. V. G. Yelisseyev stressed the great interest represented by A. A. Zavarzin Jr's work, since it is devoted to the study of differentiation of the epithelium and connective tissue in the course of embryogenesis. In order to thoroughly understand the changes which are taking place in tissues in embryogenesis, it is important to know the rate of development of the

nervous and endocrine systems during each given period. He emphasized the point that reticulin fibres do not change into others, while the pre-collagen fibres (also argyrophilic) change into collagen ones. Prof. S. I. Shchelkunov thinks that data cited in Zavazin's report indicate the presence of tissue determination already in the early stages of histogenesis.

The report of V. A. Vasil'yeva (Leningrad) was devoted to the substantiation of determination of the corneal epithelium. During regeneration and transplantation the changes in the corneal and conjunctival epithelium are uniform, while during the process of histogenesis the most important changes take place under conditions of the closed cavity of the conjunctival sac. Under these conditions changes take place in the conjunctival epithelium (glandular elements appear), together with the development of muscles and neural elements connected with these structures.

The following demonstrations were devoted to the development of cutaneous derivatives: Ye. A. Zagoruchenko (Odessa) -- "On the Regeneration of Hair and its Age-Related Reconstruction in Human Beings during the Post-Embryonal Period." F. N. Kucherova (Rostov-on-Don) -- "Growth and Development of Hair Integument in Embryos and Progeny Depending on the Various Content of Sulfur Containing Proteins in the Food Regime of Mother."

The report of Ye. Sh. Gerlovin (Leningrad) was devoted to the role of function in the morphogenesis of secretory structures of the oral cavity of vertebrate animals and man in ontogenesis and phylogenesis under experimental and pathological conditions.

In the report were cited facts which show that the small and large salivary glands of the oral cavity manifest signs of peculiar secretory activity during embryogenesis, and that during the process of development a change in their functional importance takes place. Based on this, the ideas were subjected to criticism according to which tissues in embryogenesis do not represent functioning structures. In experiments on the transplantation of protein (parotid) and mucose (submaxillary) salivary glands in the oral cavity of adult cats and kittens the role of the function of transplant healing was demonstrated and the importance of heredity in tissue plasticity. The report also demonstrated the effect of prolonged, chronic, gradually developing disturbance of the function of the human salivary glands under pathological conditions (in the salivary calculus disease) on the regeneration of glandular tissues. The cited data indicate a considerable mutability and plasticity of the secretory structures under changed conditions of their functioning. According to the speaker, the tissues are functioning structures at all stages of onto- and philo-genesis under experimental and pathological conditions, and that these structures adapt themselves to the concrete environmental conditions, and that the tissue adaptation takes place in close contact with their heredity (determination)

which reflects the history of their development.

In answer to questions by Prof. Z. S. Katsnel'son, Ye. Sh. Gerlovin stated that the reactive properties of protein and mucose glands are different, and so is the role of myoepithelial elements.

Prof. V. G. Yelisseyev mentioned that one must speak not of the adaptation of tissues but of the reaction of the organism to changed conditions. Ye. D. Logachev (Kemerovo) thinks that the study of specialized tissues is of great interest. Specialized parasitary forms undergo a definite regression but at the same time there is in them a development of vitally important tissues which are formed at an early stage. The early development of vitally important tissues and organs confirms the principle of asynchronic development which has been corroborated in a number of instances. The tissue determination must be studied in its comperative aspect.

The report of Prof. K. D. Filatova (Dnepropetrovsk) was devoted to the regeneration of the epithelial elements of the respiratory tracts under conditions of pollution with quartz and iron ore dust. Under the influence of chronic action of dust, destructive and later regenerative processes develop in the epithelium of the mucose membrane of the respiratory tracts followed by an indirect metaplasia with the formation of a multilayer, flat, horny epithelium which replaces the multiple row ciliary epithelium; an intense development of beaker-like mucose cells and glandular hypertrophy takes place. Subsequently, also atrophic processes may develop in the grandular apparatus.

During the debate V. P. Mikhaylov cited the conclusions of V. G. Garshin on the typical character of metaplasia in the multiple row epithelium. S. I. Shchelkunov stressed the practical importance of Filatova data. The metaplasia of respiratory tracts has been studied in detail, particularly in regard to regeneration. The speaker presented new data on chronic continuous experiments where a true metaplasia takes place. However, it would be interesting to elicit what actually takes place under these conditions with the breathing part of the lung.

The report of A. Ya. Friedenshteyn (Moscow) was devoted to a histochemical analysis of changes of the transitory epithelium of the unirary bladder under experimental conditions, and of their connection with the osteogenetic activity of the epithelium. Upon the administration of one percent iodine solution into the cavity of the urinary bladder (the experiments lasted three months), a cornification, mucose degeneration, and bone formation take place within the wall of the bladder. At this, a change of carbohydrate metabolism takes place in the transitory epithelium, as well as the formation of glycoproteids and mucopolysaccharides. Presumably, the osteogenetic activity takes place in the intermediary products of transformations of polysaccharides which obtain access to the underlying connective tissue. According to the speaker, under the

above mentioned conditions the epithelium retains its specific histochemical characteristics and, consequently, it does not undergo metaplastic changes.

During the debate Prof. V. P. Mikhaylov noted that mucose formation is characteristic not only of the enterodermal but of the other epithelia as well (in norm and pathology) independently of their origin. V. G. Yeliseyev noted that glycogen is of considerable importance in an inflammatory reaction, for it is liberated at the seat of inflammation following the destruction of leucocytes. The transitory epithelium also liberates polysaccharides which cause osteoformation. Thus, glycogen serves not only as reserve nutritive material but also represents an important factor in the formation of reactive structures. S. I. Shchelkunov called attention to the regular distribution of phosphatase and glycogen in the cells of the transitory epithelium which indicates the peculiar conditions of functioning of the epithelium. It is important to take into account the extreme proximity of the transitory epithelium to the blood vessels -- a fact which the speaker had not mentioned.

In the report of V. G. Petrova (Leningrad) substantial data were presented on the histochemical analysis of changes in the kidneys following the ligation of one or both ureters; changes of RNA in the cytoplasm of the cells of the urinary canaliculi were demonstrated, as well as the reduction of the content and the depolymerization of DNA in the cellular nuclei. Upon the removal of the ligature, the return of the cytological picture to norm takes place. There are cytochemical signs present of the enhancement of the function of the epithelium of the nephron on the side opposite the ligature.

Prof. Shchelkunov expressed regret that the changes had not been followed in all sections of the nephron. However, in her concluding statement V. I. Petrova mentioned that she is already in possession of the corresponding data.

A demonstration by I. A. Shumova (Leningrad) was devoted to a detailed cytochemical analysis of changes in the epithelium of the mammary gland and uterine cervix in cancer, and a demonstration by Yuan Li-yun (Leningrad) relating to changes in nucleic acids during the regeneration of the epithelium of the mucose membrane of the tongue. At the demonstration by N. G. Gorikov (Rostov-on-Don) data were presented on the transformation of a homotransplant of the musoce membrane of the esophagus of rabbit embryos and adults in the anterior eye chamber. According to the author, the esophageal epithelium is of entodermal origin.

Prof. N. A. Shevchenko\* thinks that this demonstration indicates the side adaptation mutability of the esophageal epithelium. However, the author does not offer an analysis of conditions which

\*He took part in the discussions at the morning session 17 April on the reports and demonstrations made on 16 April



determine the differentiation of various epithelia and does not show the junction between the multilayer and multiple epithelium.

Prof. A. G. Knorre mentioned that, in order to understand tissue evolution, of great interest are the data of excellent demonstrations presented by N. A. Butskaya (Leningrad) -- "The Role of the Cellular and Tissue Structures of the Testis in the Realization of Adaptations Connected with the Type and Economy of Spawning of Fish," by O. F. Saku and M. N. Chistova (Leningrad) -- "Histophysiological Analysis of Glands of Hatching in Fish in Connection with the Conditions of Embryogenesis" and by I. A. Barannikova (Leningrad) -- "Histophysiology of the Pre-Optical Hypophyseal Neurosecretory System in Salmon during the Period of the Anadromic Migration and Spawning." These and other works from the laboratory of N. L. Gerbil'skiy clearly demonstrate the role of the cellular and tissue structures in the realization of type adaptations and the importance of the ecologo-histophysiological approach to the understanding of the problems of tissue evolution.

A demonstration by A. I. Saliychuk (Odessa) was devoted to the changes of tissues of chorionic fibres of a human embryo in extrauterine pregnancy.

In summarizing the session, Chairman Prof. M. Ya. Subbotin (Novosibirsk) noted that the speakers had employed in their works new methods and had outlined new paths of investigation. The presented data not only clarify facts which are already known, but also offer the opportunity to penetrate into the intimate processes which condition the morphological changes. The problem of interconnection of tissue systems in the process of differentiation which is of considerable importance to the understanding of tissue determination, has been thoroughly elucidated in the reports. A. A. Zavarzin long ago saw one of the causes of determination in intertissue integrations connected with the emergence of multicellularity.

The fourth session (morning 17 April) continued with reports devoted to determination and plasticity of epithelial tissues.

There was considerable interest created by the report of Prof. Z. S. Khlystova (Orenburg) on the importance of the method of tissue cultivation in the organism, suggested by F. M. Lazarenko, for the study of regeneration, reactivity, and plasticity of tissues under normal and changed conditions. Parallel with the study of a number of epithelial tissues in a healthy organism which supplemented the Lazarenko data, the author cited new facts on the growth of tissues and organs when the endocrine and neural regulation is impaired. Of particular interest are data relating to the fact that the epithelium of the mammary gland undergoes hypertrophy in pregnant females only, while in non-pregnant ones it takes place only after the removal of the hypophysis, which indicates the high determination and dependence of its growth on hormonal correlations.

Upon transplantation of the submaxillary salivary gland into a denervated area, its epithelium loses its property of elimination of foreign bodies, its propensity for submersion growth increases and its functional differentiation is inhibited.

Prof. Z. S. Katsnel'son thinks that the different reaction of tissues of the recipient under conditions of denervation, particularly the difference in cell division under these circumstances, presents special interest.

Prof. T. A. Girgor'yeva (Moscow) noted that the author's conclusion on the increase of inflammation indennervation corresponds to her experimental data on deafferentation.

Prof. S. I. Shchelkunov stressed the fact that the extensive data presented in the report of Khlystova indicates that she and her co-workers are successfully developing the F. M. Lazarenko trend.

The report of the Doctor of biological sciences N. I. Grigor'yev (Leningrad) summarized many years of comparative histological and experimental studies of the epithelium of the intestinal type in vertebrate animals. The author noted that the intestinal type epithelium, though it is characterized by high mutability, does not nevertheless change into an epithelium of a different type, least of all into that of connective tissue. The indications available in the literature on the multiple-row character of the epithelium of the gall bladder, intestines, and liver proved to be incorrect. The fallacy of this point of view is clearly manifested during the study of this epithelium under normal as well as experimental conditions in regeneration, transplantation, and cultivation outside of the organism of various animals. The author subjected to criticism the works of G. Ilias who incorrectly refers to the epithelium of lower vertebrates and sauropsides as a double layer type. Comparative and experimental study of this epithelium indicates that it always retains its typical monolayer character. Control studies by the author fully exclude the possibility of transformation of the epithelium into connective tissue.

Prof. Katsnel'son supports the criticism of new ideas on the structure of the liver. In birds, for example, the columnar structure of the liver is clearly visible. A. G. Knorre thinks that the question of specialization of various epithelia of the intestinal type is too sharply posed by Girgor'yev. For instance, Men Wen showed the possibility of mutual transition of islands of the endocrine apparatus into exocrine parts of the pancreas and the development of the latter from the epithelium of the excretory ducts. Prof. V. G. Yelisseyev did not find himself in accord with the strict specificity of various types of the intestinal epithelium. Thus, during the regeneration process liver cells may develop from the epithelium of the bile ducts. Prof. Shchelkunov stressed the fact that Grigor'yev had shown in extensive factual material the

specificity of diverse varieties of the intestinal-type epithelium. In the regeneration of the liver its cells divide themselves and form a regenerate. In experiments by Shchelkunov with a view toward obtaining experimental hepatitis and cirrhosis the increased growth of liver cells was also observed.

In the report of N. M. Zhukova (Leningrad) on the material treated with the use of histochemical methods, regeneration characteristics of the epithelium of various zones of gastric mucosa were shown. Following an injury to the epithelium of the caedial, fundial and pyloric zones of the stomach, the mucose membrane is regenerated with complete preservation of the structure of the initial epithelium specific to each zone. The course of the process of regeneration of the epithelium and glands of each of the above-mentioned zones has its peculiarities connected with the specificity of their epithelium.

Prof. Shevchenko noted that the study of the provisory regeneration of the epithelium is important. Of greatest interest is the regeneration in operative intervention under pathological conditions. Katsnel'son thinks that the epithelial regeneration must not be separated from the regeneratoon of connective tissue. He called attention to the fact that at the fundus of a cat's stomach are two sections with various glands, a circumstance which means that the character of regeneration of the fundus glands must also be different. Yelisseyev asked the speaker: "If upon injury one observes a complete regeneration of the structure of the initial epithelium specific to each gastric section, how can it be related to the works of Lazovskiy who had observed the reorganization of remaining parts following the resection of a considerable part of the stomach?" Shchelkunov noted the correctness of Shevchenko's statement on the differences in the structure of the epithelial regenerate depending upon conditions of injury. It is important to study the dynamics of tissue changes. The experiment must be such as to explain what is encountered in life.

N. M. Zhukova in her concluding statement explained the difference of her findings from those of Lazovskiy as due to a different arrangement of experiments. L. A. Sharay (Leningrad) spoke on the changes of determination of the gastric epithelium under conditions of repeated prolonged injuries; the formed regenerate dedifferentiates itself, while the epithelial layer loses some of its specific characteristics. In experiments lasting over two months one observes a gradual loss by the epithelium of the mucose membrane of the fundus of the stomach of its property of differentiation in the direction of the principal, lining, and mucoid cells. Of special interest are changes in the epithelium of the stomach shortly after the cessation of a continuous effect of stimuli, which indicate the fairly stable character of gastric changes originating under conditions of chornic experiments.

The report of L. I. D'yachenko (Samarkand) notes that upon separation of the two N. vagi, a dedifferentiation of the living and, especially, the principal cells takes place. According to the speaker, the impulses coming from n. vagus maintain the differentiation of the cellular composition of gastric glands and ensure their normal functional performance. Absence of such impulses leads to a change in glandular functions and a structural reorganization of highly differentiated cells.

T. V. Ponomareva (Leningrad) submitted interesting data on the specificity of structure and reactivity of the epithelium of various sections of the small intestines under conditions of regeneration. Histochemical methods were employed in this work. The speaker noted the diverse property of epithelial filia and crypts in forming a regenerate. The filiform epithelium is more resistant to mechanical injury and possesses a slight capacity for plastic potencies. In the restoration of the mucose membrane of the duodenum the epithelium of Brunner glands takes part, and its regenerate possesses a number of specific properties which distinguish it from the intestinal epithelium.

Grigor'yeva noted that the reports of the young comrades (N. M. Zhukova, L. A. Sharay and T. V. Ponomareva) showed good content and arrangement of experiments, and were well illustrated. But one must not limit oneself to the one task in view only, but should study processes in their broader aspects, in particular -- study changes in the connective and other tissues.

The report of S. M. Tyurin (Ivanovo) was devoted to age-related changes of the epithelium of large intestines of humans and certain mammalia. The author demonstrated the structure characteristics of the epithelium of the large intestines in various mammalia and man, as well as the localization of cambial elements.

In the report of Prof. E. D. Bromberg (Khar'kov) "Experimental Neurodystrophy and its Course in Various Reactivities of the Organism" original data were presented on neurodystrophic processes in the tissues of the oral cavity in mechanical and chemical injuries of the second and third branches of n. trigeminus of rabbits. The experiments were conducted under various conditions of the nervous system. The author thinks that there are compensatory mechanisms and a considerable plasticity of the nervous system, as well as phenomena of self-regulation of tissues, which in nerve injury contribute to the normalization of tissues and the processes which take place in them. In anergic, normergic, and hyperergic reactivity the reactivity of the compensatory mechanisms varies. The emergence and course of neuro-dystrophic process, following injury of the branches of the trigominal nerve, is to a great extent conditioned by the reactive state of the organism.

V. G. Yelisseyev noted that the Bromberg report is very

interesting, especially its data on bone changes in injuries of the trigeminal nerve. The experiments of the speaker are of great practical value. Prof. S. M. Milenkov (Minsk) noted that in the work of Prof. Bromberg attention is paid to the auxiliary elements of the nervous system, the role of which has also been investigated by V. V. Portugalov.

In the report of L. B. Berlin (Leningrad) comparative histological data on the regeneration and transplantation of the epidermis in vertebrates were presented, and the different type of epithelial regeneration in lower and higher vertebrates and human beings was pointed out. In a groundling and frog the epithelial regenerate grows along the fibrin without a scab, while in mammalia and man it grows along the granulation tissue, the development of which proceeds faster than in lower vertebrates. In regeneration the epithelial structure changes considerably. The epidermal regenerate covers the wound with a complex layer and, despite considerable structural change, retains its inherent multiple-layer character and vertical anisomorphic structure which reflects its stable determination.

A demonstration by Ye. D. Logachev (Kemerovo) was devoted to the boundary function of tissues of the internal medium in parasitic flatworms. On the basis of the study of age-related changes and certain pathological states in a number of cestodes and certain plerocercoids a small differentiation of their tissues was elicited.

In speaking of Logachev's demonstration, A. G. Knorre noted that substitution of various tissues by the derivatives of another embryonic leaf is observed also in other animal species, for example, in bryozoa whose intestines and stomach are lined with ectodermal epithelium.

The chairman Prof. G. A. Nevmyvaka (Perm') noted the considerable importance of the reports. He indicated, however, that little account was taken in the reports of the neurological factors. It is to be regretted that the report of L. Il D'yachenko was not accompanied by a demonstration of preparations.

The fifth session (17 April, evening) was devoted to the reactivity and determination of muscular tissues.

Prof. L. V. Polezhayev (Moscow) in his report "Determination and Plasticity of Tissues in the Determination Process in Mammalia" stated that determination is understood in two ways: as a state and as a process. The basic rule of determination in ontogenesis has been established at present. Therefore, the current and leading problem in experimental morphology at the present time is to ascertain the rules of the adaptive dependence of determination on the changing conditions of existence of the organisms. The limits of plasticity are at present defined in various ways. A. V. Polezhayev described the development of bone tissue in a

defect of the osseous part of the cranium. A transplantation of bone shavings mixed with blood was made into the defect area; here the shavings underwent lysis and caused the development of bone within the connective tissue. The formation of the latter takes place in the presence of the hard cerebral membrane.

According to the speaker, the cardiac muscle does not regenerate under ordinary conditions. However, upon the treatment of animals with hydrolsates and extracts prepared from the heart of rats, the entire injured area fills up with newly formed muscle tissue. Its source are myoblasts originating from polyblasts. The factor which induces the transformation of polyblasts into myoblasts is represented by the disintegrating muscle fibers, and the disintegration process is enhanced by the hydrolsates.

K. A. Lavrov stressed the fact that it is impossible to speak of an absolute determination of tissue structures. P. P. Runyantsev thinks that the work is insufficiently documented. S. I. Shchelkunov called attention to the inexpediency of using osseous-blood material in cranial injuries. And the transformation of polyblasts into muscle fibers is also doubtful. The potencies of polyblasts had been thoroughly studied as far back as during Maximov's time. In order to prove the possibility of their transformation a meticulous study of the entire process is essential.

The report of Prof. K. A. Lavrov (Roston-on-Don) was devoted to the role of plastic structures in the interstitial and inter-tissue transformations which take place in a tumor process. The author transplanted muscular tissue or other inductors into the cerebrum or iris. In this connection, according to the speaker, there appear in the neural tissue peculiar structures analogous to the glial or neural cells and possessing transverse striae analogous to the striated structure of skeletal muscles. The speaker calls such structures "hybrides." These hybrides may show the predominance of neural or muscular characteristics. In the cerebellar tumors one encounters Purquine cells grown together with the striated fibers. These fibers grow by way of attachment of an amorphous substance to their ends. Under normal conditions one can observe on the example of the iris muscles the differentiation of muscular tissue from a rudiment of the nervous system. One can observe an analogous phenomenon in malignant tumors.

V. P. Mikhaylov thinks that the picture presented by Lavrov can be treated as the superposition of neural elements on muscular ones. According to Shchelkunov, the author's data are not convincing. The biological essence of the hybrides is not clear, it has not been demonstrated how the development of these formations takes place. One can not find these formations in nature, neither are they seen on the preparations. One can see on the preparations the disintegration and superposition of striated muscle fibers.

Prof. L. V. Polezhayev considers Lavrov's data new and

correct. After the invagination of the posterior part of the nerve leaf, muscles are differentiated in the latter. Kleinenberg in his time brought forward the idea of the existence of neuro-muscular formations at various stages of evolution.

In his concluding statement Lavrov noted that one does not speak of the accretion of neural and muscular fibers, but of an induction which causes the reorganization of neural fibers as a result of which the latter acquire a striated pattern. A. A. Zavarzin wrote that though there are no non-differentiated neuro-muscular fibers at present, it does not signify that they can not exist during the process of evolution. In the cerebellum of a dolphin there are normally striated muscular fibers. According to Lavrov, if everybody had agreed at once with the cited data, there would arise the need of refuting the modern ideas existing in histology.

P. P. Rumyantsev (Leningrad) cited a number of new data corroborating Zavarzin's ideas on the morphological specificity of the myocardium as compared to skeletal muscles. The data on the absence of lamellar inserts in lower vertebrates and their concurrence with telophragms must be revised in connection with the new electronic microscopic studies. The speaker called attention to the peculiarities of the mitotic division of the muscle fibers of the cardiac muscle. However, the question of the cellular structure of the myocardium can not as yet be considered indisputable. The myocardium grows during regeneration (especially its subepicardial layer) in the form of myosimplasts. The specificity of the myocardium is expressed in its comparatively low regenerating properties, its considerably higher resistance to high temperature, etc. The speaker thinks that the contradiction which A. A. Zavarzin and N. G. Khlopin make between the cardiac and skeletal muscles is justified and requires a still more thorough study. Kochetov observed that the bands formed during the development of muscular fibers do not continue uninterruptedly, but originate in the form of little columns. In cultures the lamellar inserts are formed in the bulges of the telophragms in the isolated columns of the myofibrils. The symplastic structure of the myocardium is secured during the ontogenesis and unifies the cardiac and somatic musculature. K. A. Lavrov thinks that at present one can not as yet treat the myocardium as a cellular type structure. The data of electronic microscopic analysis of the myocardium are not sufficiently convincing as yet.

P. P. Rumyantsev noted in response to Kochetov's retort that bands in the fibers are formed not only during the early stages of development but also later, though very infrequently. The basic proof of the cellular structure of the myocardium is the property of its nuclei of mitotic division.

A. A. Kolosova (Rostov-on-Don) demonstrated the peculiarities of the myocardial regeneration in various vertebrates. In amphibiae one observed the property of the myogenic scar tissue of further differentiation, particularly of formation of fibers with smooth and striated myofibrils.

During the debate V. P. Mikhaylov expressed an agreement with the Lavrov laboratory on the characteristics of the cardiac mesenchyma taking into account the fact that mesenchyma is an aggregate concept. Kochetov thinks that in studying myocardial regeneration it is important to consider the character of trauma. Myoblasts do appear after an injury but it is not known whether they develop muscle fibers. Thus, in a punctate injury of the cardiac wall a complete restoration of the myocardium takes place. Lavrov emphasized the point that, the higher the class of vertebrates, the most complete is the reaction of the myocardium to an injury. Rumyantsev thinks that in the work of A. A. Kolosova the myocardial reaction to trauma was for the first time thoroughly studied in its comparative aspect. Of the greatest interest are data on the various levels of reactive property. However, Rumyantsev does not agree with the conclusion regarding the augmentation of the regenerative activity of the myocardium in phylogenesis. In frogs the regenerative properties of the myocardium are much higher than in mammalia.

The report of G. V. Aleksandrovskaya (Moscow) was devoted to the analysis of the accretion of the striated muscles after their subperineural transplantation into the regenerating nerve. As a result, one observed a differentiation of muscular tubulae, formation of striated muscle fibers, and the establishment of a contact between the regenerating nerve and the newly formed muscle fibers.

Mikhaylov emphasized the point that these experiments represent a practical interest from the point of view of calculating the most favorable conditions needed for the development of tissue in their multicentric growth.

In the report of A. A. Klishov (Leningrad) were presented data on the development characteristics of various groups of muscles of man in embryogenesis. The author noted that at the early stages of histogenesis the cells of the myotome form argyrophilic fibers. Toward the sixth week of development the myoblasts change into myosimplasts, and starting with the seventh to eighth week muscular tubules are formed which are subsequently differentiated into striated muscle fibers.

In closing the session Chairman Prof. B. Yu. Abreytis (Kaunas) noted the urgency of the problems raised in the report.

Data presented by L. V. Polezhayev, P. P. Rumyantsev, A. A. Kolosova and G. V. Aleksandrovskaya must be worked out so that they could be introduced into practice.



The sixth and final session took place on 18 April. The greatest interest was created by the report of Prof. A. L. Shabadash (Moscow) "Functional Plasticity of the Nervous System and the Myth of its Radioresistance." The effect of small doses of ionizing radiation on the organism during their prolonged use is insufficiently studied. Almost in all recent summaries on radiobiology a classification of tissues according to their radiosensitivity is given, and the muscular and neural tissues are considered the least sensitive. This is surprising, since neural and muscular systems, the most reactive in the organism, allegedly appear the most radioresistant. According to the speaker, this is incorrect. Blum evaluates the sensitivity of the nervous system to ionizing radiation on the basis of staining of slides with hematoxylin and eosin which is a gross error. In order to obtain a final solution of the problem of the radioresistance of the nervous system it is important to determine the changes in cytological indices. It is necessary to take into account the fact that during irradiation the processes in this tissue develop in connection with the time element, and that parallel with affliction-phenomena there are taking place in it also reparation processes. Physiologists noted the polymorphism of these changes, the non-specificity of the affliction picture, and finally the impairment of the nervous system. The existing pathological indices of the affliction of the nervous system are incomplete. Biochemical changes take place in it considerably earlier than morphological ones. The histochemical analysis of the neural tissue changes in irradiation showed considerable changes in the isoelectric points and in the alkaline and acid groups. In the first place, there is the impairment of the processes of oxidizing phosphorylation and of the bond between the phosphate groups and the ribonucleoproteids. Physiologically it is manifested in a catastrophic excitability of nervous cells, a desorganization of their work, and in a continuous flow of pathological impulses.

Changes in the afferent part of the nervous system appear very early, when there is still no inkling of changes in the hemopoiesis. The histochemical methods make possible the study of functional changes in the nervous system.

During the debate, Corresponding-Member of the Acad Med Sci USSR Prof. B. A. Dolgo-Saburov (Leningrad) emphasized the importance of the data by A. L. Shabadash who, using histochemical methods, observed the minutest changes in the nervous system in irradiation. However, he called attention to the fact that the nervous system is the regulating system of the organism and changes in it must reflect themselves in the entire organism. In animals subjected to 600 r irradiation a typical radiation sickness takes place. Under these conditions a collateral circu-

lation develops which indicates that the nervous system retains its plastic properties.

Bibikova (Moscow) thinks that, if no one doubts the reaction of the central nervous system to any stimuli, it seems strange to insist on its radioresistance. This point of view is especially popular in the foreign literature; besides, the majority of researchers over there in general do not study the central nervous system. Therefore, the data on the histochemical study of changes in the nervous system are particularly important.

Prof. Ya. A. Vinnikov stressed the point that it is important to study at the expense of what is the compensation of nervous afflictions effected and how it is regulated. The efforts of scientists must be unified in the solution of this problem. Prof. S. Ya. Zalkind noted that A. L. Shabadash lifted the curtain on functional cyto- and histo-chemistry which is of great importance in the study of the reaction of various cellular forms to various influences (toxins, viruses, and antibiotics).

The report of Z. Kh. Rakhmatullin and R. V. Sadriyeva (Samarkand) was devoted to nerve endings of the nasal mucose in atrophic catarrhal conditions. This problem is of practical importance in Central Asia in connection with the large incidence of afflictions of the respiratory tract mucosa under these conditions. The following demonstrations were also devoted to changes in nerve endings under pathological conditions: A. S. Sadikov (Samarkand) "Histology of the Esophageal and Gastric Nerves of Dogs in Norm and in Leishmaniasis," and D. A. Amindzhanova (Samarkand) "Histomorphology of the Ganglions of the Solar Plexus of Man in Certain Infectious Diseases."

The report of Ye. F. Voronkina (Rostov-on-Don) and demonstrations by Kh. A. Karapetyan and F. A. Adamyan (Yerevan) were devoted to plasticity and compensatory adaptation reactions of the nervous system of the spinal cord under experimental and pathological conditions. Of special interest are the data of the latter demonstration the authors of which showed, by means of morphological and physiological methods, the great possibilities of compensation of impaired functions in puppies following separation of the spinal cord as  $3/4$  of its transverse section, while in adult animals there is no restoration of functions under these circumstances. The authors explain it by the fact that the specialization and localization of the conducting system of the spinal cord in puppies is expressed in a lesser degree than in adult dogs.

The effect of the nervous system on tissue processes was the subject of the following demonstrations: G. S. Abiyev (Baku) "Effect of Medicinal Sleep on the Origin and Development of an Inflammatory Reaction," M. A. Kalugina (Novosibirsk) "On the Problem of Neural Regulation of Differentiation of Connective

Tissue of the Umbilical Cord" and S. A. Shibkova (Rostov-on-Don) "On the Trophic Effect of Hasserian Node on the Retina."

A. A. Zorina (Karaganda) reported on the state of the neural elements of the uterus and vagina in pregnancy and during the post-partum period. The disintegration of certain afferent fibers and their receptory endings previous to labor the speaker interprets as an adaptation which protects the central nervous system from numerous and diverse impulses. The uterine and vaginal nervous apparatus during labor and the post-partum period undergoes substantial morphological changes of an adaptive character.

Corresponding Member of the Acad Med Sci USSR Prof. B. A. Dolgo-Saburov took part in the debate on the report of A. A. Zorina and noted that changes in the female genital organs during pregnancy and during and after labor are known. I. P. Pavlov long time ago observed changes in reflexory activity of female animals during pregnancy. Dolgo-Saburov also elicited during pregnancy changes in the receptors of various reflexogenic ion zones and of the synaptic apparatus of the central nervous system. Ya. L. Karaganov noted the reaction of the reflexogenic zones of the vascular bed to the influence of sex hormones.

T. L. Studentsova (Kazan') thinks that the speaker did not take into account the age-related characteristics, and did not present the description of the neural elements of the uterine cervix, and is of the opinion that one can not compare the sexual cycle of human beings and dogs.

N. M. Kolesnikov (Baku) showed changes in the connective tissue of various organs in cancer.

The report of N. V. Popova (Moscow) was devoted to the analysis of changes of the ectoplasmatic process in fibroblasts in certain reactions of the connective tissue to the administration of leucocytary and native serum of the blood of a horse. Following the administration of leucocytary serum there takes place in the cells of the fibroblast series a substantial change in the metabolism of the nucleic and cytoplasmatic RNA and in the character of the ectoplasmatic process. The author indicates the possibility of utilization of this serum for the purpose of intervention in the processes of physiological regeneration of tissues.

Shchelkunov noted that at the present time the pathologists are immersed in the study of changes in the interstitial substance (collagen) but they say nothing of the cells which form this interstitial substance. Therefore, this problem ought to attract greater attention of researchers, and it is very important that the report of N. V. Popova is devoted to this problem.

The report of Ye. D. Logachev and B. P. Bruskin (Kemerovo) was devoted to the analysis of the reactivity of the connective

tissue of mollusks under the effect of a biological stimulus (sporocyst and cat fluke redia). The dynamics of the connective tissue reaction of mollusks during the penetration of sporocysts was thoroughly investigated. The fibre-porous capsule formed around the larva of the parasite is regarded by the authors as a specific reaction of the connective tissue of the mollusk developed in the process of phylogenesis of the tissue interrelations of the host-parasite system.

Prof. S. Ya. Zalkind reminded listeners that A. A. Zavarzin had always stressed the necessity of studying the histology of nonvertebrates, since unfortunately the comparative histology of these animals so far has been insufficiently studied in our country.

The report of Prof. Z. S. Katsnel'son (Leningrad) was devoted to the possibility of a direct transformation of cartilagenous cells into osseous ones under conditions of ectonic osteogenesis. Upon the study of the histogenesis of heterotropic ossification in domestic animals, one observes (in rabbit's ear) pictures of direct transformation of cartilagenous cells into osseous ones. The elastic cartilage in the areas of bone-formation changes preliminarily into a hyaline cartilage which may directly (without preliminary destruction) change into bone tissue; at this, cartilagenous cells walled-in into an oxyphilic bone substance change into branched osseous cells. According to A. Ya. Friedenshteyn, the data cited by Katsnel'son are unconvincing. The speaker did not avail himself of the works of A. N. Studitskiy and A. N. Rumyantsev which had shown that the argument on cartilage metaplasia is based on the methods used. The speaker's preparations can be interpreted for, as well as against, metaplasia.

Prof. K. A. Lavrov (Rostov-on-Don) noted that his laboratory had completed a work on the substitution of cranial bone defects with a preserved cartilage. Under these conditions one can observe the direct metaplasia of cartilage into bone.

Prof. Ya. A. Vinnikov observed in a man's larynx a vigorous ossification following an injury. In the opinion of Prof. S. Ya. Zalkind the Katsnel'son data are convincing. He expressed disagreement with the statements of Friedenshteyn and Vinnikov, for it is not always necessary to have new methods for the proof of debatable problems. The old methods can not be cast aside.

Prof. S. I. Shchelkunov pointed out that Prof. Dolgo-Saburov some time ago described the transition of cartilage into bone in the area where a tendon is fastened to the bone. One can observe a clear transition in these areas, not a conversion of cartilage into bone.

Prof. Katsnel'son (in his concluding remarks) stated

that he is not a supporter of extensive metaplasias, but that the facts at his disposal indicate the probable conversion of cartilage into bone.

B. I. Kardasevich (Odessa) reported on artificial osteogenesis in muscles and in injuries of cranial bones by means of auto- and homo-transplantation of segments of the urinary bladder wall into the injured areas. Cysts were formed at the seat of transplantation lined up with a transitory epithelium, while the connective tissue surrounding the cysts was being converted into bone.

A. Ya. Friedenshteyn (Moscow) emphasized the point that in the Kardasevich report a very important problem had been tackled and important data of practical value had been obtained. It is necessary to detail in the future the process of bone tissue histogenesis in the transplantation of the urinary bladder to the seat of the defect of cranial bones.

In the report of A. D. Smirnov data were presented on the regeneration of the wall of the carotid and femoral arteries in adult dogs upon their separation with subsequent application of a circular suture. The restoration of the entirety of the vascular wall is effected through the proliferation of the endothelial elements which manifest a most vigorous mitotic activity of the connective tissue elements of the adventitia which form a connective tissue scar, and later, of the cells of the subendothelial layer and the smooth muscular elements.

N. A. Kolesnikova (Moscow) emphasized the valuable fact that in the work of Smirnov the regeneration of the entire vascular wall had been followed through.

The report of G. Ya. Grafova was devoted to the specificity of vascular endothelium and its reactivity. Upon slight injury the endothelium became dedifferentiated and assumed the appearance of a porous syncytium. It obtained its specific structure only after the covering of the surface of the wound. In the case of extensive injuries endothelial regeneration, under the action of a hypertonic solution of sodium chloride, takes place with the participation of connective tissue cells the differentiation of which leads to the formation of endothelium. These data indicate the possibility of converting connective tissue elements into endothelium and vice-versa.

Prof. K. A. Lavrov (Rostov-on-Don) noted that there was not the least doubt that endothelium and connective tissue are variously determined derivatives of mesenchyma. This fact proves that tissues are being determined not at the gastrula and neurula stages, as N. G. Khlopin and his school think.

Prof. Ya. A. Vinnikov thinks that the endothelium does not behave as a connective tissue under experimental conditions. There are works in which there is shown the presence of a vascular

rudiment in which the development of erythrocytes and vascular endothelium is strictly determined. This problem requires further study.

N. A. Kolesnikova noted that the endothelium is polymorphous also in norm. The islands of endothelium may grow smaller. A pigment may be deposited in them during their lifetime.

Prof. Shchelkunov emphasized the point that one can not consider the entire endothelium as synonymous. In fish it forms blood elements in some blood vessels, and in the liver -- reticulin fibers. In the abdominal aorta of a rabbit the endothelium lies on an elastic membrane, and in regeneration a connective tissue layer appears following the proliferation of the endothelial cells.

In closing the Conference, Corresponding Member of the Acad Sci USSR Prof. S. I. Shchelkunov noted that the Seventh Conference dedicated to the memory of Academician Aleksey Alekseyevich Zavarzin had discussed urgent problems of modern histology -- the determination and plasticity of tissues. The preceding six Zavarzin conferences had been devoted to various problems of tissue evolution which Zavarzin had urged be developed. The Seventh Conference is the largest of them all. While only histologists of Moscow, Leningrad, and a few other cities had participated in past conferences, 300 morphologists took part in the Conference, including 67 visitors from 23 cities of the country. This speaks for the fact that the Zavarzin conferences were becoming tradition. The problem of determination has hitherto been little illuminated in the literature and insufficiently discussed. Some people thought that determination is an incorrect concept, methodically harmful. S. I. Shchelkunov stressed the fact that the determination concept in the light of dialectic materialism must include all facets of the interaction of the organism and environment. A. A. Zavarzin called precisely upon this correct use of the concept.

The best resolution of the Conference must be the publication of its works.

In concluding the review of the work of this Conference, it is necessary to note that it has been devoted to the central problem of modern histology and embryology -- determination and plasticity of tissues, which has a great theoretical and practical significance to the understanding of the reactivity and plasticity of tissues under pathological conditions. This problem has been analyzed under various aspects; the reports created sharp, principal discussions which ensured a thorough discussion of the reports and demonstrations. The Conference showed the variety of methods used in the investigations (autoradiography, histo- and cyto-chemistry, culture of tissues in vitro and in the organism, trypsin-treated cultures, effect of ionizing radiation,

transplantation, denervation, antigenic analysis, etc.), as well as extensive use of the pathological data. Of importance is the successful efforts of intervention in the morphological processes (for example, works on heterotypical osteogenesis, etc.) in the interests of practice. The data submitted at the Conference enlarged the ideas of determination and plasticity of various tissues and placed before the researchers a number of new problems, particularly the problem of study of the autoinduction of tissues during postembryonic ontogenesis, the necessity for a revision and a thorough cyto- and hosto-chemical analysis of changes in the nervous system under the effect of ionizing radiation, the problem of stimulation of regeneration processes of the cardiac muscle, etc.

Certain discussion problems raised at the Conference require further study.

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